

### **REMARKS**

Claims 1-9, 11, 12, 14-16 and 18-22 were amended to address grammar issues, to adapt terminology unique to U.S. practice and to provide clarity.

Claims 17 and 23 were cancelled without prejudice.

I. Beginning on page 3 of the Office Action, claims 1-8 and 16-22 were rejected under 35 U.S.C. 112, first paragraph for an alleged want of enablement. Essentially, the Examiner took the position that not any sugar can be used. For example, the Examiner believed that an aldonic acid cannot be made if a sugar does not have a reducing end.

The rejection is traversed for the following reasons.

As noted by the Examiner, forming an aldonic acid of a saccharide is known in the art. Page 2, third full paragraph of the English language translation of the application teaches aldonic acid at the reducing end of the sugar as known in the art. Page 8, third full paragraph of the English language translation of the application teaches making aldonic acids.

The specification is read by one of ordinary skill in the art. Thus, contrary to the position of the Examiner, applicant maintains that one of skill in the art would readily know what polysaccharide starting materials can be used to make aldonic acid derivatives thereof for use in the claimed invention.

Clearly, the specification and claims set forth how to make and how to use, in light of the state of the art, the reagent for one step of the claimed invention. In view thereof, applicant maintains that the claimed invention is enabled fully and a prima facie case of non-enablement has not been made. Hence, withdrawal of the rejection is requested respectfully.

II. Beginning on page 3 of the Office Action, claims 1-22 were rejected under 35 U.S.C. 112, second paragraph for an alleged lack of distinctive language in the claims.

Several issues were raised and are discussed and traversed seriatim.

(a) The first issues relate to the words, “derivative” and “functional.”

Without capitulating to the position of the Examiner, some of the claims were reworded using equivalent terms. For example, while functional was intended, for example, to refer to a functional group, which, as known in the art, refers to a chemically reactive group, or to indicate a role, such as a biologic role, in some cases the term was removed without detracting from the scope and definiteness of the claim. In other circumstances, the term is used as an appositive part of a phrase defining a specific entity, for example, “a carbonate derivative of an alcohol.”

In any event, it is believed this portion of the rejection either is moot or is overcome.

(b) Regarding claims 12 and 13, the Examiner indicated that the phrases used therein are indefinite.

In the polymer art, there are a number of metrics that can be used and are used to characterize a preparation. As known in the polymer art, normally mean values are presented to characterize the range of species of polymer in a preparation.

The term, “number average of the mean molecular weight,” is the English language translation of the appropriate phrase presented on several occasion in the text of the underlying parental PCT application, which was filed in the German language.

Attached hereto is a copy of a dictionary-type listing providing the art-recognized definitions of, “number average molecular weight,” (page 2) and, “weight average molecular weight,” (page 3). As can be seen, each phrase is an acceptable metric for describing and defining a polymer preparation.

Also as known in the art, dividing the weight average metric by the number average metric provides a metric for the distribution of individual species in the preparation about the mean, that is, the distribution of species in the population, which the Examiner correctly indicated as the polydispersity index.

Hence, it is believed the terms set forth in claims 12 and 13 would be well recognized by one of skill in the polymer art as terms defining a polymer preparation. At the least, the artisan would recognize the terms as grammatic variants of phraseology normally used in the U.S. or as one English translation of the equivalent phrase from the German language.

(c) Finally, the Examiner raised an issue with elements of nested range.

This portion of the rejection is moot.

In conclusion, the claims are clear and distinct, and an artisan would well be able to interpret the claims and the metes and bounds thereof. Accordingly, withdrawal of the rejection is requested respectfully.

III. Beginning on page 9 of the Office Action, claims 1-11 and 14-22 were rejected under 35 U.S.C. 103(a) over Cook in view of Sommermeyer and Vallazza et al.

Cook was alleged to teach dextran derivatives of polynucleotides. The Examiner noted that Cook does not teach a dry solvent, an aldonic acid ester, particular molar ratios thereof, HES, a spiegelmer or the MW of the oligonucleotide.

To compensate for those many deficiencies, the Examiner turned to Sommermeyer for teaching HES derivatives and to Vallazza et al. for teaching aptamers.

Hence, the Examiner concluded that because the elements of the invention were known in the art, for example, it would have been predictable to combine the elements to obtain the invention.

The rejection is traversed for the following reasons.

As noted by the Examiner, Cook does not teach or suggest an aldonic acid of a polysaccharide as a reactant to conjugate a polysaccharide and a polynucleotide.

For example, Cook refers in Example 8 to a preparative method provided in Pietta et al. (Prep Biochem 14:313-329, 1984, copy submitted concurrently herewith for the convenience of the Examiner). Pietta et al. teach at page 315 use of 6-bromo hexanoic acid to form carboxyl dextrans (and not aldonic acid derivatives of dextran) which carboxyl dextrans then are bound to a protein, and not to a nucleic acid.

Cook also does not teach or suggest a carbonate of an alcohol.

Thus, it is clear Cook does not teach or suggest a plurality of elements required for the efficient conjugation of particular polysaccharides to particular polynucleotides as claimed.

Sommermeyer teaches conjugating a reducing sugar to a protein. There is no teaching or suggestion of using an aldonic acid or a carbonate of an alcohol for conjugating a polysaccharide to a polynucleotide comprising an amino group.

Hence, Sommermeyer also is fatally deficient as to the claimed invention, and does not cure the fatal deficiencies of Cook as to the claimed invention. Thus, a prima facie case of obviousness has not been made over those two references.

Valazza et al. relate to aptamers. That reference does not relate to a method of conjugating a particular polysaccharide to a particular polynucleotide as claimed.

Hence, again, a prima facie case of obviousness has not been made.

In closing, applicant wishes to point out the numerous unsuccessful attempts to conjugate a polysaccharide to a polynucleotide that were observed prior to the instant invention.

As noted in the first three full paragraphs on page 6 of the instant application, it was a surprise that activation of hydroxyl groups was not observed as expected. Instead, a specific activation of the carboxyl group of the aldonic acid was observed. Also, as noted in the fourth full paragraph on page 6, prior art methods using carbodiimide, such as, EDC, were inefficient with polynucleotides because of the negative impact of phosphates and phosphate groups on such reagents. See also the paragraph bridging pages 6 and 7, and the first three full paragraphs of the instant specification for other examples of the lack of success with prior art materials and methods. Clearly, there is no predictability in the art.

Hence, combining prior art elements in known methods did not yield predictable results. Simple substitution of one known element for another did not yield predictable results. Known techniques were inoperable in conjugating a polysaccharide with a polynucleotide. Applying known methods to obtain the claimed end result met with failure. Because there is no predictability in the art, there are no finite and predictable solutions. As there is no predictability in the art, mere predictable variations in the relevant art or in a different art are not available. Finally, there is no teaching or suggestion in the art to obtain the claimed invention.

Accordingly, the particular combination of claimed elements neither was known nor suggested in the art. Moreover, there is no predictability in the art to have made or to render the claimed invention obvious.

Thus, for those additional reasons, a prima facie case of obviousness has not been made and the rejection should be withdrawn.

**CONCLUSION**

Applicant has take steps to place the application in condition for allowance.  
Reexamination, reconsideration and withdrawal of the rejections are requested respectfully.  
Favorable consideration and early indication of allowance are solicited earnestly. If any  
questions remain, those can be directed to the undersigned at the local exchange noted below.

Respectfully submitted,

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